REMARKS

This Amendment is filed in response to the Office Action dated December 26, 2007. Claims 1-3 and 6-8 are pending in the application. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing. Please reference 112701-818 on the invoice for any such charge.

In the Office Action, Claims 3 and 7 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. According to the Office Action, an RNAi oligonucleotide is inconsistent with an RNA polynucleotide antisense to a target sequence. Applicants have amended Claims 3 and 7 to provide a polynucleotide that is a cRNA. Support for this amendment may be found in the Specification at, for example, page 10, lines 23-24. therefore no new matter has been added by this amendment. Applicants respectfully submit that the rejection under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

In the Office Action, Claims 1-3 and 6-8 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. The Office Action suggests that there is lack of support in the Specification for compositions comprising a polynucleotide antisense to gluosylceremide synthase mRNA and compositions that treat or prevent epithelial tissue damage. In support of this contention, the Office Action lists four reasons that there is no relation between the claimed composition and treating or preventing epithelial tissue damage. In contrast to the assertions at page 5, it is well known and described in the Specification that glucosylceramide synthase is associated with epithelial tissue damage, that the regulation of glucosylceramides in maintaining epithelial cell homeostasis is related to preventing/treating epithelial damage by silencing glucosylceramide synthase expression, and that reducing epithelial cell proliferation is related to preventing/treating epithelial damage.

The survival and propagation of epidermal cells damaged and/or mutated by stress in the form of UV radiation, pollutants, free radicals, chemical substances and the like leads to epithelial tissue damage. Specification, page 4, lines 3-4 and page 8, lines 9-18. Whether the damaged cells survive and propagate depends on a balance between proliferation, differentiation and apoptosis of epidermal cells. Specification, page 7, lines 28-29. This balance is regulated by lipids. Specification, page 7, line 30. In particular, ceramides inhibit cellular proliferation and induce cellular differentiation and programmed cell death, and, conversely, glycosylceramides

promote cellular proliferation and prevent cellular differentiation and programmed cell death. Specification, page 8, lines 4-6. CD_{1d} supports the continued existence of stressed cells by binding glycosylceramides. Specification, page 8, lines 7-8 and page 10, lines 13-15. Glycosylceramide synthase converts ceramides into glycosylceramides. Therefore, genetic modification or deletion of the glucosylceramide synthase mRNA to reduce the availability of glycosylceramides to CD_{1d} binding blocks the function of CD_{1d} to support the survival and propagation of damaged epidermal cells, thus preventing or treating epithelial tissue damage.

Furthermore, as pointed out in the Specification at page 10, lines 19-21, the nucleotide sequence of glucosylceramide synthase, and thus its mRNA, is known and disclosed in Ichikawa et al. PNAS 93 (1996) p. 4642. Moreover, as provided in detail in a previous response dated June 18, 2007, designing and manufacturing an RNA polynucleotide antisense to a known sequence does not require undue experimentation. Therefore, one of skill in the art would be enabled by the knowledge in the art and the description in the Specification to practice the claimed invention. Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §112, first paragraph, is improper and should be withdrawn.

For the foregoing reasons, Applicants respectfully submit that the application is in condition for allowance and earnestly solicit reconsideration of same.

Respectfully submitted,

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